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Research Article

# A Rapid DMeyer-CWT Method Application to the Spectrophotometric Data for the Quantification of Losartan Potassium and Hydrochlorothiazide in a Binary Mixture

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ABSTRACT

This paper outlines a precise, swift, and convenient spectrophotometric method based on the continuous wavelet transform methodology for the estimation of losartan potassium and hydrochlorothiazide in tablets. The continuous wavelet transform method is based on the use of DMeyer (DMEY-CWT). When the original UV spectra of losartan potassium and hydrochlorothiazide are studied, it is clear that their spectra closely overlap. The analysis was completed successfully without any pre-separation using the created DMEY-CWT approach. The calibration equations for losartan potassium measurement and hydrochlorothiazide determination were obtained at 257.6 nm and 268.4 nm for losartan potassium, 250.1 nm and 263.8 nm for hydrochlorothiazide. The developed approaches were evaluated for their validity and practicality.

## 1. Introduction

Researchers today are attempting to meet the demands of better scientific measurements and to evolve more efficient processes to boost the accuracy of existing analytical methods in order to attain the desired analytical results across a range of disciplines, such as those noted above. [1-3].

To get more chemical data and minimize the complexity of multicomponent substance analysis, LC and CE procedures were utilized in combination with various spectroscopic systems (independent approaches, notably LC-MS and CE-MS). Furthermore, these combined unit approaches are expensive and time consuming to analyze [4-6]. For analytical purposes, analytical procedures such as spectrophotometry [7], mass-spectrometry [8], chromatography [9], electrophoresis [10], electrochemistry [11], and their combined devices have been utilized. Because of the difficulties of the aforementioned separation techniques or combination analyzers, analytical chemists prefer to employ spectroscopic methods (rather than separation techniques) to enable rapid and low-cost analysis. Continuous wavelet transform (CWT) approaches for spectrophotometric data are becoming increasingly popular since they may be employed in the study of components in complicated systems without the requirement for any separation step.

As a result, CWT approaches can provide appropriate answers in such instances. [12-14].

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The aim of this study is to propose a new signal processing approach based on the simultaneous quantitative detection of losartan potassium (LOS) and hydrochlorothiazide (HCT) in tablets without the usage of a separation step using CWT and zero crossing methodology [15]. In pharmacological and biological investigations, several analytical techniques for the determination of LOS and HCT have been published, including spectrophotometric methods [16-19], spectrofluorometric methods [20], and chromatographic methods [21-25].

## 2. General Methods

A Shimadzu UV-1601 dual-beam UV-VIS spectrophotometer with a constant gap width of 2 nm was used to analyze the absorption spectra of mixes and tablet solutions in the spectral range 200-305 nm.

### 2.1. Commercial tablet

A pharmaceutical tablet (HYZAAR® Tablet, MSD Ind., Istanbul, Türkiye, batch no:401042301) including 50 mg LOS and 12.5 mg HCT per tablet was gathered from the Turkish market.

### 2.2. Standard solutions

By dissolving 25 mg of each drug in 100 mL of methanol, standard LOS and HCT stock solutions were created, respectively. From standard stock solutions for each active component, a calibration with a range of 4.0-26.0 µg mL-1 for LOS and 2.0-24 µg ml-1 HCT in solvent was made for spectrum analysis.

### 2.3. Sample solutions preparation

Twenty LOS and HCT tablets were weighed and pulverized for testing. Add methanol to a 100 ml volumetric flask along with an equal amount of powder. The flask's contents were swirled mechanically. The supernatant is diluted with methanol to its final concentration after filtering. Ten times this process was carried out.

## 3. Results and Discussion

Applying the DMEY-Continuous wavelet transform (DMEY-CWT) approach to the spectra of LOS and HCT in mixtures and preparations for the simultaneous assay is the goal of this work. The UV spectra of the tablet solution and the LOS and HCT standards were measured between 200 and 305 nm, as shown in Figure 1.

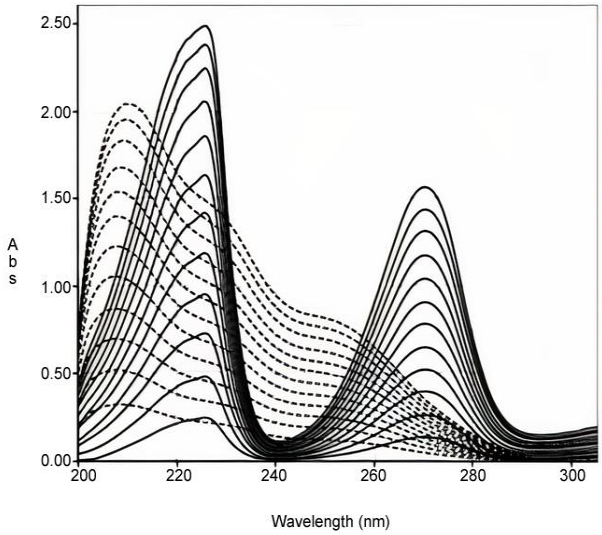


**Figure 1.** The UV-Absorption spectra of 4.0-26 µg mL-1 LOS (---) and 2.0-24 µg mL-1 HCT (─) in methanol

### 3.1. DMEY continuous wavelet transform method (DMEY-CWT)

Using methanol as the solvent, calibration mixtures were prepared with linear concentration ranges of 4.0–26 µg mL–1 for LOS and 2.0–24 µg mL–1 for HCT in order to analyze artificial mixtures and tablets containing LOS and HCT compounds by the DMEY–CWT technique. These calibration solutions' initial UV spectra were captured at wavelengths between 200 and 305 nm, with = 0.1 nm intervals. The LOS and HCT spectra were subjected to the DMEY-CWT technique (Figure 2). Table 1 displayed the regression equation, correlation coefficient, and associated statistical information.

The quantitative analysis of synthetic mixtures was used to validate the calibration equation for the DMEY-CWT technique. Table 2 displays the recovery outcomes together with the relative standard deviation. In the application of these methods, DMEY-CWT method was applied

directly to UV spectra and DMEY-CWT amplitudes were measured at 257.6 nm and 268.4 nm for LOS and 250.0 nm and 263.8 nm for HCT in the concentration range of 4.0-26.0 µg/mL for LOS and 2.0-24.0 µg/mL for HCT by using zero-cut technique in the obtained DMEY-CWT spectra and calibration graphs were obtained by linear regression. Table 1 displays the results of the regression analysis.

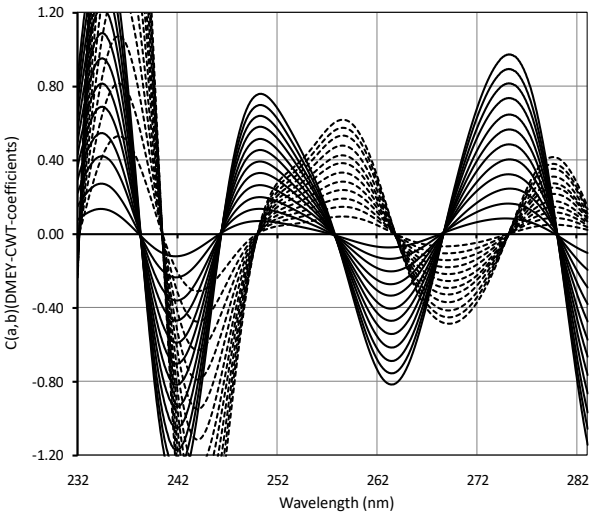


**Figure 2.** DMEY-CWT spectra obtained by transforming the UV absorption spectra of LOS (---) and HCT (—)

**Table 1.** Statistical outcome for the DMEY-CWT method

| **Method** | **DMEY-CWT** | | | |
|---|---|---|---|---|
| **Parameter** | **LOS** | **HCT** | | |
| **λ (nm)** | 257.6 | 268.4 | 250.1 | 263.8 |
| **m** | $2.34x10^{-2}$ | $-1.86x10^{-2}$ | $3.14x10^{-2}$ | $-3.41x10^{-2}$ |
| **n** | $-1.67x10^{-3}$ | $8.64x10^{-3}$ | $1.12x10^{-2}$ | $2.32x10^{-3}$ |
| **r** | 0.9999 | 0.9997 | 0.9999 | 0.9998 |
| **SE(m)** | $1.43x10^{-3}$ | $1.37x10^{-3}$ | $1.27x10^{-4}$ | $1.83x10^{-4}$ |
| **SE(n)** | $1.17x10^{-4}$ | $1.43x10^{-4}$ | $1.39x10^{-3}$ | $1.69x10^{-3}$ |
| **SE(r)** | $2.80x10^{-3}$ | $3.43x10^{-3}$ | $3.03x10^{-3}$ | $4.37x10^{-3}$ |
| **OD** | 0.69 | 0.82 | 0.50 | 0.56 |
| **LOQ** | 2.29 | 2.75 | 1.65 | 1.85 |

### 3.2. Validation of the Proposed Methods

A validation set consisting of 24 artificial mixture solutions in methanol at different concentrations within the linear working range of 4.0-26.0 µg/mL for LOS and 2.0-24.0 µg/mL for HCT was prepared. This validation set evaluated the DMEY-CWT method's precision and accuracy. Table 2 displays the results obtained after using the DMEY-CWT approach to synthetic combinations produced as a verification set.

The prepared solutions were utilized for intra-day and inter-day tests in order to evaluate the accuracy and precision of the DMEY-CWT technique. Precision and accuracy evaluations were applied daily at three different concentrations. The results can be seen in Table 3.

**Table 2.** Recovery outcome calculated by using artificial mixtures

| DMEY-CWT | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Added (μg mL$^{-1}$)** | | **Found (μg mL$^{-1}$)** | | | | **Recovery (%)** | | | |
| | | LOS (μg mL$^{-1}$) | | HCT (μg mL$^{-1}$) | | LOS | | HCT | |
| LOS | HCT | 257.6 nm | 268.4 nm | 250.1 nm | 263.8 nm | 257.6 nm | 268.4 nm | 250.1 nm | 263.8 nm |
| 4 | 6 | 3.94 | 4.18 | 5.94 | 5.99 | 98.4 | 104.5 | 99.0 | 99.9 |
| 6 | 6 | 5.65 | 5.92 | 5.97 | 5.86 | 94.2 | 98.7 | 99.6 | 97.7 |
| 8 | 6 | 7.78 | 8.07 | 5.98 | 5.80 | 97.2 | 100.9 | 99.7 | 96.6 |
| 10 | 6 | 9.80 | 10.03 | 6.04 | 5.86 | 98.0 | 100.3 | 100.7 | 97.7 |
| 12 | 6 | 11.77 | 12.01 | 5.97 | 5.80 | 98.1 | 100.1 | 99.5 | 96.7 |
| 14 | 6 | 13.94 | 14.15 | 5.88 | 5.76 | 99.6 | 101.1 | 97.9 | 96.0 |
| 16 | 6 | 15.97 | 16.22 | 6.02 | 5.82 | 99.8 | 101.4 | 100.4 | 97.0 |
| 18 | 6 | 18.18 | 18.50 | 6.11 | 5.81 | 101.0 | 102.8 | 101.8 | 96.9 |
| 20 | 6 | 20.02 | 20.40 | 5.87 | 5.91 | 100.1 | 102.0 | 97.8 | 98.5 |
| 22 | 6 | 22.06 | 22.45 | 5.94 | 6.00 | 100.3 | 102.0 | 99.0 | 99.9 |
| 24 | 6 | 24.04 | 24.48 | 5.98 | 5.88 | 100.2 | 102.0 | 99.6 | 98.1 |
| 26 | 6 | 25.94 | 26.42 | 5.98 | 5.87 | 99.8 | 101.6 | 99.7 | 97.8 |
| 24 | 2 | 24.02 | 24.01 | 2.17 | 2.04 | 100.1 | 100.0 | 108.7 | 101.8 |
| 24 | 4 | 24.15 | 24.19 | 4.11 | 4.05 | 100.6 | 100.8 | 102.8 | 101.2 |
| 24 | 6 | 24.18 | 24.40 | 6.19 | 5.95 | 100.8 | 101.6 | 103.1 | 99.2 |
| 24 | 8 | 24.00 | 24.02 | 8.12 | 7.92 | 100.0 | 100.1 | 101.5 | 99.0 |
| 24 | 10 | 24.20 | 24.46 | 10.15 | 9.76 | 100.8 | 101.9 | 101.5 | 97.6 |
| 24 | 12 | 23.96 | 24.22 | 12.14 | 11.58 | 99.8 | 100.9 | 101.1 | 96.5 |
| 24 | 14 | 24.35 | 24.85 | 14.00 | 13.52 | 101.5 | 103.6 | 100.0 | 96.6 |
| 24 | 16 | 24.27 | 24.65 | 15.96 | 15.49 | 101.1 | 102.7 | 99.7 | 96.8 |
| 24 | 18 | 24.26 | 24.80 | 17.72 | 17.12 | 101.1 | 103.3 | 98.4 | 95.1 |
| 24 | 20 | 24.36 | 24.43 | 19.84 | 19.05 | 101.5 | 101.8 | 99.2 | 95.3 |
| 24 | 22 | 25.24 | 24.09 | 21.73 | 20.75 | 105.2 | 100.4 | 98.8 | 94.3 |
| 24 | 24 | 24.73 | 24.11 | 23.26 | 23.85 | 103.1 | 100.4 | 96.9 | 99.4 |
| | | | | | Mean | 100.1 | 101.5 | 100.3 | 97.7 |
| | | | | | SD | 2.06 | 1.31 | 2.36 | 1.87 |
| | | | | | RSD | 2.35 | 1.30 | 2.35 | 1.91 |

**Table 3.** Intra-day and inter-day outcome by the DMEY-CWT method

| | **Added (μg mL$^{-1}$)** | **Found (μg mL$^{-1}$)** | **SD** | **RSD** | **RE** | **Recovery (%)** |
|---|---|---|---|---|---|---|
| **Intra-day Results** | | | | | | |
| **LOS** 257.6 nm | 4 | 4.08 | 0.04 | 1.09 | 2.12 | 103.0 |
| | 16 | 16.20 | 0.38 | 2.36 | 1.26 | 101.8 |
| | 20 | 20.32 | 0.41 | 2.01 | 1.62 | 101.9 |
| **HCT** 250.1 nm | 4 | 3.94 | 0.09 | 2.38 | -1.54 | 98.9 |
| | 16 | 16.17 | 0.36 | 2.23 | 1.06 | 99.4 |
| | 20 | 20.03 | 0.30 | 1.48 | 0.14 | 99.6 |
| **LOS** 268.4 nm | 4 | 3.95 | 0.07 | 1.76 | -1.37 | 98.3 |
| | 16 | 15.87 | 0.22 | 1.39 | -0.81 | 100.0 |
| | 20 | 20.13 | 0.29 | 1.42 | 0.63 | 100.2 |
| **HCT** 263.8 nm | 4 | 3.89 | 0.17 | 4.35 | -2.80 | 99.5 |
| | 16 | 15.96 | 0.15 | 0.95 | -0.22 | 100.3 |
| | 20 | 19.80 | 0.45 | 2.28 | -1.01 | 98.2 |
| **Inter-day Results** | | | | | | |
| **LOS** 268.4 nm | 4 | 4.12 | 0.04 | 1.04 | 3.00 | 98.3 |
| | 16 | 16.28 | 0.21 | 1.32 | 1.77 | 100.0 |
| | 20 | 20.39 | 0.38 | 1.86 | 1.94 | 100.2 |
| **HCT** 263.8 nm | 4 | 3.96 | 0.06 | 1.54 | -1.08 | 99.5 |
| | 16 | 15.90 | 0.24 | 1.52 | -0.62 | 100.3 |
| | 20 | 19.92 | 0.25 | 1.25 | -0.41 | 98.2 |
| **LOS** 268.4 nm | 4 | 3.93 | 0.07 | 1.78 | -1.70 | 98.3 |
| | 16 | 16.00 | 0.16 | 1.00 | 0.00 | 100.0 |
| | 20 | 20.03 | 0.23 | 1.14 | 0.16 | 100.2 |
| **HCT** 263.8 nm | 4 | 3.98 | 0.07 | 1.76 | -0.53 | 99.5 |
| | 16 | 16.05 | 0.14 | 0.90 | 0.28 | 100.3 |
| | 20 | 19.64 | 0.44 | 2.26 | -1.80 | 98.2 |

The interfering effects of tablet excipients on LOS and HCT were tested using a standard addition methodology before the DMEY-CWT method was used to the commercial tablet composition. Table 4 presents the findings.

| | Added (μg mL$^{-1}$) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | LOS | | | | | | HCT | | | | | |
| | 2 | | 6 | | 10 | | 2 | | 8 | | 12 | |
| No. | Found (μg mL$^{-1}$) | | | | | | Found (μg mL$^{-1}$) | | | | | |
| | 257.6 | 268.4 | 257.6 | 268.4 | 257.6 | 268.4 | 250.1 | 263.8 | 250.1 | 263.8 | 250.1 | 263.8 |
| 1 | 1.99 | 2.03 | 5.71 | 5.84 | 10.04 | 9.92 | 1.96 | 2.05 | 7.83 | 8.03 | 11.95 | 12.02 |
| 2 | 1.94 | 2.08 | 5.85 | 5.90 | 10.24 | 9.86 | 1.93 | 2.07 | 7.83 | 7.84 | 11.94 | 12.27 |
| 3 | 1.98 | 2.09 | 5.89 | 5.84 | 10.22 | 9.75 | 1.93 | 1.96 | 8.19 | 8.06 | 11.84 | 12.18 |
| 4 | 2.01 | 2.07 | 5.96 | 6.06 | 10.31 | 9.86 | 1.93 | 1.98 | 7.84 | 8.09 | 12.02 | 12.11 |
| 5 | 2.00 | 2.02 | 6.06 | 5.95 | 10.35 | 9.96 | 1.91 | 2.01 | 7.80 | 7.90 | 11.79 | 11.99 |
| | Recovery (%) | | | | | | | | | | | |
| No. | LOS | | | | | | HCT | | | | | |
| | 257.6 | 268.4 | 257.6 | 268.4 | 257.6 | 268.4 | 250.1 | 263.8 | 250.1 | 263.8 | 250.1 | 263.8 |
| 1 | 99.6 | 101.3 | 95.2 | 97.3 | 100.4 | 99.2 | 98.1 | 102.6 | 97.9 | 100.3 | 99.6 | 100.2 |
| 2 | 97.1 | 103.9 | 97.5 | 98.3 | 102.4 | 98.6 | 96.3 | 103.7 | 97.8 | 98.0 | 99.5 | 102.3 |
| 3 | 98.8 | 104.3 | 98.2 | 97.4 | 102.2 | 97.5 | 96.6 | 98.1 | 102.4 | 100.7 | 98.6 | 101.5 |
| 4 | 100.6 | 103.6 | 99.3 | 101.0 | 103.1 | 98.6 | 96.5 | 99.1 | 98.0 | 101.1 | 100.2 | 100.9 |
| 5 | 99.9 | 101.0 | 101.0 | 99.2 | 103.5 | 99.6 | 95.6 | 100.5 | 97.5 | 98.7 | 98.2 | 100.0 |
| Mean | 99.2 | 102.8 | 98.2 | 98.6 | 102.3 | 98.7 | 96.6 | 100.8 | 98.7 | 99.8 | 99.2 | 101.0 |
| SD | 1.32 | 1.6 | 2.16 | 1.5 | 1.21 | 0.8 | 0.91 | 2.3 | 2.05 | 1.3 | 0.78 | 0.9 |
| RSD | 1.33 | 1.5 | 2.20 | 1.5 | 1.18 | 0.8 | 0.94 | 2.3 | 2.08 | 1.3 | 0.79 | 0.9 |
| RE | -0.79 | 2.8 | -1.76 | -1.4 | 2.33 | -1.3 | -3.39 | 0.8 | -1.29 | -0.2 | -0.78 | 1.0 |

**Table 4.** Standard addition results for DMEY-CWT method

By subtracting the amount of LOS and HCT from the tablets, recovery and other calculations for LOS and HCT were carried out. Five replicas were used for these surveys, with three different concentration grades.

### 3.3. Tablet Analysis

Table 5 displays the results obtained by applying the suggested technique to the LOS-HCT commercial preparation solutions. Results have been obtained successfully for quantifying tablets containing LOS and HCT. When the DMEY-CWT method was applied to commercially accessible tablets, there was no interaction with the tablet excipients in the determination of the concerned substances.

**Table 5**. Tablet assay by the DMEY-CWT method (50.0 mg LOS and 12.5 mg HCT per tablet)

| | mg/tablet | | | |
|---|---|---|---|---|
| | LOS | | HCT | |
| | 257.6 nm | 268.4 nm | 250.1 nm | 263.8 nm |
| Mean | 49.82 | 50.04 | 12.65 | 12.44 |
| SD | 0.47 | 0.81 | 0.11 | 0.15 |
| RSD | 0.93 | 1.63 | 0.83 | 1.18 |
| SE | 0.15 | 0.26 | 0.03 | 0.05 |
| CL | 0.29 | 0.50 | 0.07 | 0.09 |

## 4. Conclusion

CWT offers new possibilities and alternative ways for the resolution of mixtures of active compounds with overlapping absorption spectra. One of the main advantages of CWT approach is the simultaneous data reduction and de-noising for the signal analysis.

In our case, this DMEY-CWT approach provides higher peak amplitude, less noise, and sharper peaks then the other wavelet families and having flexible and versatile properties gives a good resolution for mentioned binary pharmaceutical dosage form. The spectrum analysis of synthetic mixtures and tablet formulations comprising LOS and HCT has been successfully carried out using the DMEY-CWT method that we have developed, to briefly explain the study.
When the spectra overlap in the same spectral region, as they do in this study, this newly developed approach can be used without the need for pre-separation (see Figure 1). To demonstrate the reliability and practicality of the method, it was carried out using analytical validation parameters. We believe that the DMEY-CWT method that has been developed is a promising approach for the measurement of related compounds.

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The authors contributed equally to the study.

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The authors of the paper declare that they comply with the scientific, ethical and quotation rules of SAUJS in all processes of the paper and that they do not make any falsification on the data collected. In addition, they declare that Sakarya University Journal of Science and its editorial board have no responsibility for any ethical violations that may be encountered, and that this study has not been evaluated in any academic publication environment other than Sakarya University Journal of Science.



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